WHAT IS CLAIMED IS:

1. A method for site-directed mutagenesis comprising the steps of:

providing two terminal tailed primers comprising an anchor portion and a portion having nucleotide sequences respectively complementary to each end of a gene to be mutated;

annealing the complementary portion of said terminal tailed primers and a set of mutagenic primers to template DNA in a single step;

synthesizing a mutant strand by primer extension and ligation; and

amplifying said mutant strand by polymerase chain reaction.

2. The method of claim 1, wherein said method is used to mutate 5 nucleotides simultaneously.

3. The method of claim 1, wherein said method is used to mutate 10 nucleotides simultaneously.

4. The method of claim 1, wherein said method is used to mutate more than 10 nucleotides simultaneously.

5. The method of claim 1, wherein said method is used to mutate 20 nucleotides simultaneously.

6. The method of claim 1, wherein said method is used to mutate 30 nucleotides simultaneously.

7. The method of claim 1, wherein said method is used to mutate 40 nucleotides simultaneously.

8. The method of claim 1, wherein said method is used to mutate 50 nucleotides simultaneously.

9. The method of claim 1, wherein said method is used to mutate more than 50 nucleotides simultaneously.

10. The method of claim 1, wherein said complementary nucleotide sequences of said terminal tailed primers are 25 nucleotides in length.

11. The method of claim 1, wherein said complementary nucleotide sequences of said terminal tailed primers are less than 25 nucleotides in length.

12. The method of claim 1, wherein said complementary nucleotide sequences of said terminal tailed primers are more than 25 nucleotides in length.

13. The method of claim 1, wherein each said anchor portion of said terminal tailed primers comprise at least one restriction endonuclease site.

14. The method of claim 1, wherein each said anchor portion of said terminal tailed primers comprise at least three restriction endonuclease sites.

15. The method of claim 1, wherein said set of mutagenic primers comprises one mutagenic primer for each desired mutation.

16. The method of claim 1, wherein said set of mutagenic primers comprises one mutagenic primer for two or more desired mutations.

17. The method of claim 1, wherein said two or more desired mutations are located less than 25 nucleotides apart.

18. The method of claim 1, wherein said primer extension is performed using a DNA polymerase.

19. The method of claim 18, wherein said DNA polymerase comprises T4 DNA polymerase.

20. The method of claim 18, wherein said DNA polymerase comprises T7 DNA polymerase.

21. The method of claim 18, wherein said DNA polymerase comprises *E.coli* DNA polymerase I.

22. The method of claim 18, wherein said DNA polymerase comprises the Klenow fragment of DNA polymerase I.

23. The method of claim 18, wherein said DNA polymerase comprises Moloney Murine Leukemia Virus reverse transcriptase.

24. The method of claim 18, wherein said DNA polymerase comprises *Pfu* DNA polymerase.

25. The method of claim 18, wherein said DNA polymerase comprises *Tli* DNA polymerase.

26. The method of claim 18, wherein said DNA polymerase comprises *Bst* DNA polymerase.

27. The method of claim 18, wherein said DNA polymerase comprises *Taq* DNA polymerase.

28. The method of claim 18, wherein said DNA polymerase comprises *Pwo* DNA polymerase.

29. The method of claim 18, wherein said DNA polymerase comprises *Tth* DNA polymerase.

30. The method of claim 18, wherein said DNA polymerase comprises *Tfl* DNA polymerase.

31. The method of claim 1, wherein said ligation is performed using a DNA ligase.

32. The method of claim 31, wherein said ligase comprises T4 DNA ligase.

33. The method of claim 31, wherein said ligase comprises T7 DNA ligase.

34. The method of claim 31, wherein said ligase comprises *Pfu* DNA ligase.

35. The method of claim 31, wherein said ligase comprises *Tth* DNA ligase.

36. The method of claim 31, wherein said ligase comprises *Tsc* DNA ligase.

37. The method of claim 31, wherein said ligase comprises *Taq* DNA ligase.

38. The method of claim 31, wherein said ligase comprises an NAD-dependent DNA ligase.

39. The method of claim 1, wherein said polymerase chain reaction is performed using a DNA polymerase.

40. The method of claim 39, wherein said DNA polymerase comprises *Pfu* DNA polymerase.

41. The method of claim 39, wherein said DNA polymerase comprises *Pwo* DNA polymerase.

42. The method of claim 39, wherein said DNA polymerase comprises *Tli* DNA polymerase.

43. The method of claim 39, wherein said DNA polymerase comprises *Tth* DNA polymerase.

44. The method of claim 39, wherein said DNA polymerase comprises *Tfl* DNA polymerase.

45. The method of claim 1, wherein said polymerase chain reaction is performed using a DNA polymerase blend comprising at least two DNA polymerases.

46. The method of claim 45, wherein said DNA polymerase blend comprises *Taq* DNA polymerase and a proofreading DNA polymerase.

47. The method of claim 1, wherein said template DNA is double-stranded DNA.

48. The method of claim 1, wherein said template DNA is single-stranded DNA.

49. The method of claim 1, wherein said mutagenic primers comprise a three-fold molar excess over said terminal tailed primers.

50. The method of claim 1, wherein said mutagenic primers each have a G or C at their 3' ends at the location at which DNA synthesis is initiated.

51. The method of claim 1, wherein said mutagenic primers are 5'-phosphorylated.

52. The method of claim 1, wherein said terminal tailed primers are 5'-phosphorylated.